Disclosures. **All authors:** No reported disclosures.

689. Therapeutic Efficacy of CB-012, a Novel Cloudbreak Antiviral Fc-Conjugate (AVC) in Lethal Mouse Models of Influenza A (H1N1) and Influenza B (Victoria)

James Levin, PhD; Allen Borchardt, PhD; Thanh Lam, PhD; Wanlong Jiang, PhD; Zhi-Yong Chen, PhD; Joanne Fortier, BSc; Suzanne Akers-Rodriguez, BSc; Karin Amundson, BSc; Joanna Donatelli, BSc; Simon Döhrmann, PhD; Jason Cole, PhD; Les Tari, PhD; Cidara Therapeutics, San Diego, California

Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs
Thursday, October 3, 2019: 12:15 PM

Background. In 2018, the World Health Organization estimated up to 650,000 influenza-related respiratory deaths occur annually. Cidara therapeutics is developing a novel class of potent, long-acting antiviral Fc-conjugates (AVCs) against influenza that in a single molecule combine a surface-acting antiviral agent with the Fc domain of a human IgG1 antibody. AVCs function by inhibiting viral replication while simultaneously engaging the immune system, providing a multimodal mechanism of action. Here we present efficacy data on an AVC development candidate against influenza A and B.

Methods. Efficacy studies were conducted in female BALB/c mice (6–8 weeks) challenged intranasally with 3x the LD_{95} of influenza A/Puerto Rico/8/1934 (H1N1) or B/Malaysia/2506/04. CB-012 or CB-012b (CB-012 with slightly modified Fc) was administered as a single intravenous (IV) dose 2 hours after challenge. Oseltamivir was dosed orally, twice daily for 5 days in the influenza A study. Vehicle and appropriate Fc controls were included. Body weights (BW) and mortality were monitored for 2 weeks; animals with 20% BW loss, or moribund, were scored as a death.

Results. In an initial study of CB-012 against influenza A, a single IV dose of 0.4 mg/kg was fully protective and statistically significant compared with the Fc control (P = 0.0027). In contrast, mice treated with oseltamivir at 5 mg/kg twice daily for 5 days were not protected; only the higher 20 mg/kg dose was fully protective. Importantly, mice treated with CB-012 (0.4 mg/kg) showed a transient BW loss of 1% compared with 14% in mice of the oseltamivir (20 mg/kg) group, although treatment was initiated at the same time. In a second study against influenza B, CB-012b was fully protective with a single IV dose at 0.3 mg/kg (P = 0.0027). In contrast, vehicle and Fc control groups reached mortality by day 6. BW loss in the CB-012b 0.3 mg/kg group was transient and <4% overall during the study.

Conclusion. The novel AVCs CB-012 and CB-012b demonstrated robust efficacy in multiple influenza models. In conjunction with previous findings against influenza A (H3N2), the data on CB-012 support its potential as a candidate against seasonal influenza. The continued development of CB-012 for the prevention and treatment of influenza is warranted.

Disclosures. **All authors:** No reported disclosures.

690. Activity of a Novel Polymyxin Analog, QPX9003, Tested Against Resistant Gram-Negative Pathogens, Including Carbapenem-Resistant *Acinetobacter*, *Enterobacterales*, and *Pseudomonas*

Mariana Castanheira, PhD[1]; Jill Lindley[1]; Holly Huynh[1]; Rodrigo E. Mendes, PhD[1]; Olga Lomovskaya, PhD[2]; [1]JMI Laboratories, North Liberty, Iowa; [2]Qpex Biopharma, San Diego, California

Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs
Thursday, October 3, 2019: 12:15 PM

Background. Multidrug resistance (MDR) among Gram-negative (GN) organisms and the limited active therapeutic options against these pathogens are matters of worldwide concern. Polymyxins are cationic peptides that act on the bacterial cell membrane and have good activity against GN organisms, including MDR strains. We evaluated the activity of QPX9003, a novel polymyxin analog with an improved safety profile over current polymyxins, against a large collection of resistant GN isolates collected worldwide.

Methods. Susceptibility testing was performed by reference microbroth dilution against 2,518 GN organisms for QPX9003, colistin (COL), levofloxacin, tigecycline, gentamicin, amikacin, meropenem, cefepime, piperacillin–tazobactam, and ceftazidime–avibactam. Isolates included 1,000 *Pseudomonas aeruginosa* (PSA) enriched for MDR, 503 carbapenem-resistant *Acinetobacter baumannii* (CRAB), and 1,105 *Enterobacterales* (ENT).

Results. QPX9003 had potent activity against PSA isolates enriched for resistance against β-lactam/β-lactamase inhibitor combinations and was 4-fold more potent than COL ($MIC_{50/90}$, 0.25/0.25 mg/L vs. $MIC_{50/90}$ of 1/1 mg/L). QPX9003 was also more potent than COL against the panel of CRAB with $MIC_{50/90}$ of 0.125/1 mg/L and 0.5/4 for QPX9003 and COL, respectively. QPX9003 had a modal MIC of 0.06 mg/L against a large collection of ENT isolates resistant to cephalosporins and/or carbapenems ($MIC_{50/90}$, 0.06/16 mg/L). QPX9003 activity was identical against 508 carbapenem-resistant *Enterobacterales* (CRE; $MIC_{50/90}$, 0.06/16 mg/L) isolates and 511 *Klebsiella pneumoniae* isolates ($MIC_{50/90}$, 0.06/16 mg/L) in this collection. *Escherichia coli* isolates were considerably more sensitive to QPX9003 ($MIC_{50/90}$, 0.06/0.12 mg/L) compared with *K. pneumoniae* isolates. Activity of QPX9003 and COL was similar against ENT. Other comparator agents had limited activity against PSA, CRAB, and CRE isolates.

Conclusion. QPX9003 had activity against this collection of highly resistant GN isolates and was particularly active against the PSA and CRAB isolates. QPX9003 is a promising new-generation polymyxin agent.

	% of isolates at MIC								MIC (mg/L)	
Organisms (no. tested)	0.03	0.06	0.12	0.25	0.5	1	2	4	50%	90%
Enterobacterales (1,015)	16.8	67.7	79.5	80.6	81.4	82.1	82.6	83.6	0.06	16
K. pneumoniae (511)	19.2	73.6	78.1	79.1	80.2	80.8	81.6	83.0	0.06	16
E. coli (297)	9.1	67.3	96.6	97.3	97.3	98.3	98.3	99.3	0.06	0.12
CRE (508)	21.3	68.9	74.4	75.8	77.0	77.8	78.5	79.9	0.06	16
P. aeruginosa (1,000)	1.0	5.1	29.8	95.1	99.0	99.5	99.6	99.6	0.25	0.25
Carbapenem-resistant *A. baumannii* (503)	0.4	3.6	56.5	81.5	89.7	92.4	94.6	95.0	0.12	1

Disclosures. **All authors:** No reported disclosures.

691. Activity of TNP-2092 Against Biofilms Formed by Prosthetic Joint Infection-Associated Staphylococci

Cody Fisher[1]; Suzannah Schmidt-Malan, MS[1]; Ying Yuan, PhD[2]; Shijie He[2]; Zhenkun Ma, PhD[2]; Robin Patel, MD[1]; Robin Patel, MD[1]; [1]Mayo Clinic, Rochester, Minnesota; [2]TenNor Therapeutics, Suzhou Industrial Park, Jiangsu, China (People's Republic)

Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs
Thursday, October 3, 2019: 12:15 PM

Background. Infection occurs in ~1–2% of prosthetic joint replacement surgeries, with staphylococci being the most common cause. TNP-2092 is an investigational drug composed of rifamycin and quinolizinone pharmacophores conjugated via a stable linker. Here, we determined TNP-2092's *in vitro* activity against biofilms formed by staphylococci associated with prosthetic joint infection and compared activity to that of ciprofloxacin and rifampin alone and in combination, as well as to daptomycin and vancomycin.

Methods. A total of 80 staphylococcal isolates (40 *Staphylococcus aureus* and 40 *Staphylococcus epidermidis*) were studied. Planktonic state minimum inhibitory concentrations (MICs) of TNP-2092, ciprofloxacin, rifampin, ciprofloxacin + fixed concentration (1 mg/mL) rifampin, daptomycin and vancomycin were determined following CLSI guidelines. Tween-80 (0.002%) was added to TNP-2092 to prevent drug binding to plastic plates. Minimum biofilm inhibitory concentrations (MBICs) and minimum biofilm bactericidal concentration (MBBCs) were determined as follows. Bacteria were grown in TSB to logarithmic phase and adjusted to a turbidity of 0.5 McFarland; 150 µL aliquots were transferred to individual wells of 96-well flat-bottom plates and the plates covered with 96-pegged lids. Plates were incubated on a shaker for 5 hours at 37°C. Pegged lids were rinsed using 200 µL PBS/well and placed into a microtiter plate containing serial 2-fold drug dilutions in CAMHB Plates were incubated for 20–24 hours at 37°C and MBICs read by visual turbidity. Pegged lids were rinsed with PBS and placed into plates filled with 200 µL CAMHB/well and incubated for 20–24 hours at 37°C after which MBBCs were determined by assessing visual turbidity.

Results. Results shown in the table.

Conclusion. TNP-2092 has promising *in vitro* activity against prosthetic joint infection-associated staphylococcal biofilms.

Antimicrobial Agent	*Staphylococcus* species	Planktonic Susceptibility (µg/mL)		Biofilm Susceptibility (µg/mL)			
		MIC_{50}/ MIC_{90}	MIC Range	$MBIC_{50}$/ $MBIC_{90}$	MBIC Range	$MBBC_{50}$/$MBBC_{90}$	MBBC Range
TNP-2092	*aureus*	≤0.0075/ 0.015	≤0.0075/ 0.125	≤0.0075/ 0.03	≤0.0075/ 0.06	0.5/ 2	≤0.0075/ 4
	epidermidis	≤0.0075/ 0.015	≤0.0075/ 8	≤0.0075/ 0.06	≤0.0075/ 0.25	0.06/ 0.25	≤0.0075/ 1
Rifampin	*aureus*	0.0075/ 0.015	≤0.004/ 0.25	0.0075/ 0.03	≤0.004/ 0.25	>4/ >4	0.03/ >4
	epidermidis	0.0075/ 0.125	≤0.004/ >4	≤0.004/ 0.25	≤0.004/ >4	0.125/ >4	≤0.004/ >4
Ciprofloxacin	*aureus*	8/ >128	0.25/ >128	8/ >128	0.25/ >128	>128/ >128	2/ >128
	epidermidis	2/ >128	0.25/ >128	2/ >128	0.5/ >128	>128/ >128	0.5/ >128
Ciprofloxacin* +1 µg/ml Rifampin	*aureus*	≤0.125/ ≤0.125	≤0.125/ ≤0.125	≤0.125/ ≤0.125	≤0.125/ 0.125	>128/ >128	≤0.125/ >128
	epidermidis	≤0.125/ ≤0.125	≤0.125/ 128	≤0.125/ ≤0.125	≤0.125/ 128	≤0.125/ >128	≤0.125/ >128
Daptomycin	*aureus*	0.25/ 0.5	≤0.125/ 4	1/ 2	≤0.125/ 2	8/ 16	0.03/ 64
	epidermidis	0.25/ 0.5	≤0.125/ 2	0.5/ 1	≤0.125/ 2	2/ 6	≤0.125/ >128
Vancomycin	*aureus*	1/ 2	0.25/ 4	2/ 4	0.06/ 0.25	>128/ >128	2/ >128
	epidermidis	2/ 4	0.06/ 4	2/ 4	0.03/ 0.5	64/ >128	0.06/ >128

*Ciprofloxacin concentration shown

Disclosures. Robin Patel, MD, ASM and IDSA: Other Financial or Material Support, Travel reimbursement, editor's stipends; CD Diagnostics, Merck, Hutchison Biofilm Medical Solutions, Accelerate Diagnostics, ContraFect, TenNor Therapeutics Limited, Shionogi: Grant/Research Support; Curetis, Specific Technologies, NextGen Diagnostics, PathoQuest, Qvella: Consultant; NBME, Up-to-Date, the Infectious Diseases Board Review Course: Honorarium recipient, Other Financial or Material Support; Patent on Bordetella pertussis/parapertussis PCR issued, a patent on a device/method for sonication with royalties paid by Samsung to Mayo Clinic, and a patent on an anti-biofilm substance issued: Other Financial or Material Support, Patents.

692. *In Vitro* Antibacterial Activity of Cefiderocol Against a Multi-national Collection of Carbapenem-Nonsusceptible Gram-Negative Bacteria From Respiratory Infections: SIDERO-WT-2014–2017

Sonia N. Rao, PharmD[1]; Sean T. Nguyen, PharmD[1]; Melinda M. Soriano, PharmD[1]; Jennifer M. Hayes, PharmD[1]; Meredith M. Hackel, PhD[2]; Daniel F. Sahm, PhD, D(ABMM), FAAM [2]; Glenn S. Tillotson, PhD[3]; Roger Echols, MD[4]; Masakatsu Tsuji, PhD[5]; Yoshinori Yamano, PhD[5]; [1]Shionogi Inc., Florham Park, New Jersey; [2]International Health Management Associates, Inc., Schaumburg, Illinois; [3]GST Micro LLC, Henrico, Virginia; [4]Infectious Disease Drug Development Consulting LLC, Easton, Connecticut; [5]Shionogi & Co., Ltd., Osaka, Japan

Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs
Thursday, October 3, 2019: 12:15 PM

Background. Cefiderocol (CFDC) is a new siderophore cephalosporin with potent *in vitro* activity against a broad range of Gram-negative (GN) pathogens, including carbapenem-nonsusceptible (Carb-NS) strains. We evaluated the *in vitro* activity of CFDC and comparator agents against recent clinical Carb-NS GN respiratory isolates collected from North America and Europe as part of the multi-national SIDERO-WT surveillance program.

Methods. A total of 2831 Carb-NS GN respiratory isolates collected from 2014 to 2017 were tested centrally (IHMA, Inc., Schaumburg, IL). Minimum inhibitory concentrations (MIC) were determined for CFDC, cefepime (FEP), ceftazidime–avibactam (CZA), ceftolozane-tazobactam (C/T), ciprofloxacin (CIP), colistin (CST), and meropenem (MEM) by broth microdilution and interpreted according to the 2018 CLSI guidelines. CFDC MICs were tested in iron-depleted cation-adjusted Mueller–Hinton broth, and interpreted according to the 2018 CLSI provisional breakpoints. Carb-NS strains were defined as MEM MIC of ≥2 µg/mL for Enterobacteriaceae (ENB) and of ≥4 µg/mL for nonfermenters (NF).

Results. CFDC exhibited predictable *in vitro* activity against 2807 clinically relevant Carb-NS GN isolates (214 ENB, 1086 *A. baumannii* complex, 693 P. *aeruginosa*, 794 *S. maltophilia*, and 20 *Burkholderia cepacia*) isolated from respiratory infections. CFDC was the most active agent against Carb-NS ENB with 97.7% susceptibility followed by 78.0% CZA, 59.4% CST, and 16.4% CIP. Against Carb-NS *A. baumannii* complex, CFDC demonstrated 94% susceptibility vs. 83.7% for CST. CFDC was the most active agent against Carb-NS *P. aeruginosa* with 99.9% susceptibility followed by 97.8% CST, 77.6% C/T, and 77.5% CZA. 99.7% of *S. maltophilia* and 100% of *B. cepacia* isolates had CFDC MICs of ≤4 µg/mL. The MIC_{90}s of tested compounds for clinically relevant pathogens are shown in the table.

Conclusion. In a multinational collection of Carb-NS GN respiratory isolates, CFDC demonstrated potent *in vitro* activity with MIC_{90} of ≤4 µg/mL for all clinically relevant ENB and NF. These findings suggest that CFDC can be a potential option for the treatment of respiratory infections caused by Carb-NS ENB, *A. baumannii* complex, *P. aeruginosa*, *S. maltophilia*, and *B. cepacia*.

Table.

	MIC_{90} (µg/mL)							
Organism	**N**	**CFDC**	**FEP**	**CZA**	**C/T**	**CIP**	**CST**	**MEM**
Enterobacteriaceae	214	4	>64	>64	>64	>8	>8	>64
P. aeruginosa	693	1	64	64	>64	>8	2	64
***A. baumannii* complex**	1086	2	>64	>64	>64	>8	>8	>64
S. maltophilia	794	0.25	>64	>64	>64	8	8	NA
B. cepacia	20	0.5	>64	32	>64	>8	NA	16

Disclosures. **All authors:** No reported disclosures.

693. *In Vitro* Activity of Ceftazidime–Avibactam and Comparator Agents Against *Enterobacteriaceae* and *Pseudomonas aeruginosa* Collected From Patients with Bloodstream Infections as Part of the ATLAS Global Surveillance Program, 2014–2017

Krystyna Kazmierczak, PhD[1]; Gregory Stone, PhD[2]; Daniel F. Sahm, PhD[1]; [1]IHMA, Inc., Schaumburg, Illinois; [2]Pfizer, Inc., Groton, Connecticut

Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs
Thursday, October 3, 2019: 12:15 PM

Background. Avibactam (AVI) is a β-lactamase inhibitor with potent inhibitory activity against Class A, Class C, and some Class D serine β-lactamases. The combination of ceftazidime (CAZ) with AVI has been approved in Europe and in the United States for several indications. This study evaluated the *in vitro* activity of CAZ-AVI and comparators against *Enterobacteriaceae* (*Eba*) and *Pseudomonas aeruginosa* (*Pae*) isolates collected from patients with bloodstream infections as part of the ATLAS surveillance program in 2014–2017.

Methods. A total of 53416 *Eba* and 15050 *Pae* nonduplicate clinically significant isolates, including 5155 *Eba* and 845 *Pae* isolated from bloodstream infections, were collected by 167 hospital laboratories in 36 countries in Europe, Latin America, Asia/Pacific (excluding China), and the Middle East/Africa region. Susceptibility testing was performed by CLSI broth microdilution. CAZ-AVI was tested at a fixed concentration of 4 µg/mL AVI. Meropenem-nonsusceptible (MEM-NS) *Eba* and *Pae* isolates were screened for the presence of β-lactamase genes.

Results. Susceptibility data are shown in the Table. Percentages of susceptibility (% S) to the tested agents were 0.2–2.8% lower among *Eba* and *Pae* from bloodstream infections compared with isolates from combined sources in most cases. CAZ-AVI showed potent *in vitro* activity against all *Eba* bloodstream isolates and subsets of CAZ-NS and colistin-resistant (CST-R) isolates (MIC_{90}, 0.5–2 µg/mL, 96.0–100% S). Reduced activity against MEM-NS *Eba* was attributable to carriage of class B metallo-β-lactamases (MBLs) because all MEM-NS MBL-negative isolates were susceptible to CAZ-AVI. CAZ-AVI also showed good *in vitro* activity against the majority of *Pae* bloodstream isolates (MIC_{90}, 16 µg/mL, 89.5% S). Activity was reduced against CAZ-NS, MEM-NS and CST-R subsets (53.7–85.0% S), which included isolates carrying MBLs, but exceeded the activity of CAZ and MEM against these subsets by 15–65%. CST and amikacin were the only tested comparators that demonstrated comparable or greater activity against *Pae* bloodstream isolates.

Conclusion. CAZ-AVI provides a valuable therapeutic option for treating bloodstream infections caused by MBL-negative *Eba* and *Pae* isolates.

Source	Organism/Phenotype (n)	Drug (MIC_{90} [µg/ml]/% Susceptible)									
		CAZ-AVI		CAZ		MEM		AMK		CST	
		MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S
All	*Enterobacteriaceae*, All (53416)	0.5	99.1	64	75.4	0.12	96.2	8	97.1	>4	83.2
Blood	All (5155)	0.5	98.9	64	72.6	0.12	94.9	8	96.7	>4	87.5
	CAZ-NS (1413)	1	96.0	>128	0.0	>8	82.1	32	89.6	2	90.5
	MEM-NS (262)	>128	78.6	>128	3.4	>8	0.0	>32	67.6	>4	72.9
	MEM-NS, MBL-negative (206)	2	100	>128	4.4	>8	0.0	>32	71.4	>4	72.8
	CST-R (140)[a]	2	98.6	>128	35.0	>8	60.7	32	85.0	>4	0.0
All	*P. aeruginosa*, All (15050)	8	91.2	64	76.1	>8	72.7	32	89.8	2	97.1
Blood	All (845)	16	89.5	64	77.3	>8	70.5	32	87.9	2	97.6
	CAZ-NS (192)	128	53.7	>128	0.0	>8	23.4	>32	56.8	2	96.9
	MEM-NS (249)	128	65.5	>128	41.0	>8	0.0	>32	63.9	2	96.8
	MEM-NS, MBL-negative (201)	32	80.6	>128	50.3	>8	0.0	>32	74.6	2	96.5
	CST-R (20)	32	85.0	32	70.0	>8	60.0	>32	80.0	4	0.0

CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; MEM, meropenem; AMK, amikacin; CST, colistin; NS, non-susceptible; R, resistant; MBL, metallo-β-lactamase. % Susceptible was determine using CLSI 2019 breakpoints.
[a]Excludes isolates of Proteeae and *Serratia* spp., which are intrinsically resistant.

Disclosures. **All authors:** No reported disclosures.

694. *In vitro* Antibacterial Activity of Sulbactam–Durlobactam (ETX2514SUL) Against 121 Recent *Acinetobacter baumannii* Isolated from Patients in India

Alita Miller, PhD[1]; Sarah McLeod, PhD[1]; Tarun Mathur, PhD[2]; Ian Morrissey[3]; [1]Entasis Therapeutics, Waltham, Massachusetts; [2]IHMA Inc., Gurugram, Haryana, India; [3]IHMA Europe, Monthey, Valais, Switzerland

Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs
Thursday, October 3, 2019: 12:15 PM

Background. The incidence of infections caused by multidrug-resistant *Acinetobacter baumannii* is increasing at an alarming rate in Southeast Asia and other parts of the world. Sulbactam (SUL) has intrinsic antibacterial activity against *A. baumannii*; however, the prevalence of β-lactamases in this species has limited its therapeutic use. Durlobactam (ETX2514, DUR) is a novel β-lactamase inhibitor with broad-spectrum activity against Ambler class A, C and D β-lactamases. DUR restores SUL *in vitro* activity against multidrug-resistant *A. baumannii*. Against >3,600 globally diverse, clinical isolates from 2012–2017, addition of 4 mg/L DUR reduced the SUL MIC_{90} from >32 to 2 mg/L. SUL-DUR is currently in Phase 3 clinical development for the treatment of infections caused by carbapenem-resistant *Acinetobacter* spp. The goal of this study was to determine the activity of SUL-DUR and comparator antibiotics (amikacin (AMK), ampicillin-sulbactam (AMP-SUL), cefoperazone-sulbactam (CFP-SUL) and meropenem (MEM)) against *A. baumannii* isolated from hospitalized patients in India.

Methods. A total of 121 clinical *A. baumannii* isolates from multiple hospital settings and infection sources were collected between 2016–2019 from six geographically diverse hospitals in India. Species identification was performed by MALDI-TOF. Susceptibility of these isolates to SUL-DUR (10µg/10µg) and comparator antibiotics was determined by disk diffusion using CLSI methodology and interpretive criteria, except for CFP-SUL, for which resistance was defined using breakpoints from the CFP-SUL package insert.

Results. As shown in Table 1, resistance of this collection of isolates to marketed agents was extremely high. In contrast, based on preliminary breakpoint criteria, only 11.5% of isolates were resistant to SUL-DUR.

Conclusion. The *in vitro* antibacterial activity of SUL-DUR was significantly more potent than comparator agents against multidrug-resistant *A. baumannii* isolates collected from diverse sites in India. These data support the continued development of SUL-DUR for the treatment of antibiotic-resistant infections caused by *A. baumannii*.

Table 1. Percent Resistant *A. baumannii* (N = 121)				
SUL-DUR	AMP-SUL	MEM	AMK	CFP-SUL
11.5%	90.9%	95.9%	88.4%	79.3%

Disclosures. **All authors:** No reported disclosures.

695. Activity of Imipenem–Relebactam and Ceftolozane–Tazobactam Against a Contemporary Collection of Gram-Negative Bacteria from New York City

Alejandro Iregui, MD; Zeb Khan, MD; David Landman, MD; John M. Quale, MD; SUNY Downstate Medical Center, Brooklyn, New York

Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs
Thursday, October 3, 2019: 12:15 PM

Background. Carbapenem-resistant Gram-negative bacteria are important nosocomial pathogens, and therapeutic options are often limited.

Methods. Clinical isolates were gathered during a surveillance study in 2017 involving 7 hospitals in Brooklyn, NY. Isolates underwent susceptibility testing using the agar dilution method; for the combination of imipenem-relebactam and ceftolozane-tazobactam, the concentrations of relebactam and tazobactam were fixed at 4 µg/mL. Breakpoints were defined according to CLSI criteria; for imipenem-relebactam, the breakpoint of imipenem was utilized. Isolates were screened by PCR for common carbapenemases.

Results. Overall susceptibility patterns are given in the Table. Of 1805 isolates of *E. coli* (including 4 with bla_{KPC}), 100% were susceptible to imipenem and imipenem-relebactam. Of 503 isolates of *K. pneumoniae* (including 19 isolates with bla_{KPC}), all were susceptible to imipenem-relebactam. Of 171 isolates of *Enterobacter* spp. (including 3 with bla_{KPC}), 100% were susceptible to imipenem-relebactam. Of 260 isolates of *P. aeruginosa*, 96% were susceptible to imipenem-relebactam and nearly all to ceftolozane-tazobactam. Against *A. baumannii*, the activity of imipenem-relebactam was the same as imipenem and the ceftolozane-tazobactam MIC was ≤ 4 µg/mL in 65% of isolates.

Conclusion. Imipenem-relebactam possesses promising activity against multidrug-resistant *Enterobacteriaceae* endemic to New York City. Ceftolozane-tazobactam demonstrated excellent activity against *P. aeruginosa*, including isolates resistant to carbapenems.

	MIC50	MIC90	Range	Susceptible (%)
	µg/ml			
E. coli (n=1805)				
Imipenem	0.25	0.25	≤ 0.12 - 1	100%
Imipenem/relebactam	0.125/4	0.25/4	≤ 0.015/4 – 0.5/4	100%
Ceftolozane/tazobactam	≤ 0.25/4	≤ 0.25/4	≤ 0.25/4 – >16/4	99.8%
Piperacillin/tazobactam	2/4	4/4	≤ 0.25/4 – >128/4	98.8%
K. pneumoniae (n=503)				
Imipenem	0.25	0.5	≤ 0.12 - >4	96%
Imipenem/relebactam	0.25/4	0.25/4	≤ 0.015/4 – 0.5/4	100%
Ceftolozane/tazobactam	≤ 0.25/4	1/4	≤ 0.25/4 – >16/4	96%
Piperacillin/tazobactam	4/4	8/4	≤ 0.25/4 – >128/4	96%
Enterobacter spp. (n=171)				
Imipenem	0.5	1	≤ 0.12 - 2	98%
Imipenem/relebactam	0.25/4	0.5/4	0.06/4 – 0.5/4	100%
Ceftolozane/tazobactam	0.5/4	2/4	≤ 0.25/4 – >16/4	92%
Piperacillin/tazobactam	4/4	32/4	1/4 – >128/4	89%
P. aeruginosa (n=260)				
Imipenem	2	>4	≤ 0.12 - >4	75%
Imipenem/relebactam	0.5/4	2/4	0.03/4 – >4/4	96%
Ceftolozane/tazobactam	1/4	2/4	≤ 0.25/4 – >16/4	98.8%
Piperacillin/tazobactam	8/4	128/4	2/4 – >128/4	76%
A. baumannii (n=49)				
Imipenem	0.5	>4	0.25 - >4	61%
Imipenem/relebactam	0.5/4	>4/4	0.12/4 – >4/4	
Ceftolozane/tazobactam	1/4	16/4	≤ 0.25/4 – >16/4	
Piperacillin/tazobactam	32/4	>128/4	≤ 0.25/4 – >128/4	45%

Disclosures. **All authors:** No reported disclosures.